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PARASITIC INFECTIONS AND CANCERS: ASSOCIATIVE STUDY

Rafatunisa Nahri
Sir Sayyed College, Aurangabad (M.S)
Email : rafatunisa.nahri@gmail.com

ABSTRACT: It's estimated that over 15% of malignancies worldwide are often attributed to infections; the figures are higher in developing countries to the extent of twenty-two compared to about 7% in developing countries. The incidence of malignancy an infectious cause is about 1.2 million cases per annum. This also implies that a minimum of a number of the cancers are preventable and will be a thrust area for research.This paper deals with the connection between parasitic infections and carcinogenesis and therefore the possible mechanisms involved.

KEYWORDS: Parasites, infections, Cancers, Associations.

INTRODUCTION

Medical parasitology deals with the parasites which infect man, the diseases they produce, the response generated by him against them and various methods of diagnosis and prevention. An association during which the parasite derives benefit and therefore the host gets nothing reciprocally but always suffers some injury. A parasite has lost its power of independent life. Recent advances within the fields of biology, epidemiology, and infectious diseases have led to significant revelations to clarify the connection between cancer and infective agents.

Infectious agents including parasites that have an oncogenic potential are often highly prevalent within the host population. They continue the host and removal of the parasite may end in the reversal of tumour development. However, high prevalence of parasitic infection within the overall population, their persistence within the host, co-infections with other microbes and other interacting factors like nutritional status, etc. make the establishment of relationship difficult.

Infections generally can initiate or promote carcinogenesis by any of the three main mechanisms:

1) Chronic inflammation the prolonged persistence of infective agents within the host: Phagocytes at the inflammatory site release reactive oxygen radicals and reactive nitrogen radicals having the potential to wreck DNA, proteins, and cell membranes, alter enzyme activities and organic phenomenon which successively can induce carcinogenesis. Moreover, chronic inflammation results in repeated cycles of cell damage and compensatory cell proliferation, thus promoting neoplasia.
2) Insertion of active oncogene within the host genomes: This usually occurs in oncogenic viruses. The oncogenes may inhibit tumor suppressor genes or directly stimulate mitosis.
3) Reduced immunosurveillance as a result of immunosuppression: altogether the

sorts of immunodeficiency, the relative risk of developing tumors, especially those during which viruses are known to play a task are greatly increased. The course of cancer in the immunocompromised host is usually aggressive although other risk factors remain unchanged.

Schistosomiasis

It is the second commonest parasitic infection of humans after malaria. Approximately 200 million people are infected globally in 76 countries and about 600 million are exposed to infection in tropical and subtropical regions of Africa, Asia, South America, and therefore the Caribbean. Schistosomiasis is caused by the trematode (blood flukes) of *Schistosoma*. The parasites pass their life cycle during a mammalian host and an invertebrate host, the water snails. *Schistosoma* larvae are released from the snails into the water as free-living cercariae, which penetrate the skin of the mammalian host. Here the parasites become schistosomula which migrate through the bloodstream to the liver where they mature into an adult and eventually release eggs into the bloodstream which either lodge into tissues and incite inflammatory reaction or are released within the urine or faeces. The eggs hatch in water to makemiracidia which invade snails.

Mainly five species infect humans namely,

- *S. haematobium,*
- *S. mansoni,*
- *S. japonicum,*
- *S. intercalatum,* and
- *S. mekongi.*

Most human infections are *S. haematobium* and *S. mansoni*. The adult worms of *S. japonicum* and *S. mansoni* reside within the inferior vena mesenterica although *S. japonicum* also resides within the superior vena mesenterica. *S. haematobium* inhabits the terminal venules within the wall of the bladder, the urogenital system, and therefore the pelvic plexus within the distribution of the inferior vein. However, it also can exist in perirectal venules excreting the eggs within the stool. At oviposition, the eggs are immature but miracidial maturation takes place during a few days. Soluble egg antigens (SEA) originating from the secretary glands of miracidia enclosed within eggs diffuse out through submicroscopic pores within the eggshell and induce an acute host hypersensitivity response. The immunopathology is granuloma formation around the eggs deposited within the tissues and may be a manifestation of delayed hypersensitivity. This results in pylephlebitis, peripylephlebitis, malignant hypertension, splenomegaly, oesophageal varices, haematemesis, and death. One particularly dreaded complication is cancer.

The international agency for research on cancer (IARC) considers *S. haematobium* infection a definitive explanation for bladder cancer with an associated 5-fold risk. This conclusion is predicated on ecological studies reporting strong direct correlation,

case reports, and several other case-control studies. Bladder cancer related to *S. haematobium* is histologically and pathologically distinct from non *S. haematobium* associated bladder cancer occurring in North America and Europe, the previous being an epithelial cell carcinoma, with an earlier age of onset and usually sparing the trigone of the bladder while the latter is of transitional cell type occurring within the older age bracket. Several mechanisms are suggested to elucidate the role of *S. haematobium* in bladder cancer:

- Fibrosis induced by schistosome eggs may induce proliferation, hyperplasia, and metaplasia, all of which are possible precancerous changes.
- Chronic urinary bacterial infection and production of nitrosamines from their precursors in urine, that are documented bladder carcinogens.
- Urinary stasis allowing the concentration of endogenous carcinogens resulting in their absorption from urine and exposure of the bladder epithelium.
- Raised urinary beta-glucuronidase levels originating from miracidia and adult schistosomes liberating carcinogenic amines in urine.

The evidence supporting the role of *S. japonicum* in cancer occurrence is weaker, although it's been related to both liver and colorectal cancer. Thus, presently *S. japonicum* is often considered a possible carcinogen for humans. Epidemiological and clinical studies in China and Japan support a probable role of *S. japonicum* infection together of the danger factors in hepatoma (HCC) formation. Additional risk factors include virus infection with hepatitis B (HBV) and hepatitis C viruses (HCV) and alcoholic abuse. Experimental studies have shown that cancer of the liver appears early and in larger numbers in animals experimentally infected with *S. japonicum* and given a known carcinogen. Case-control studies in China and the Philippines and epidemiological cross-sectional surveys in China have suggested both positive and negative associations. One case-control study in China showed a robust association between *S. japonicum* infection and rectal cancer but no association between *S.japonicum* infection and colonic cancer.

The link between *S. mansoni* and HCC appears to be an indirect one. Patients with *S. mansoni* have higher rates of HBV and HCV infection compared to noninfected controls.The upper exposure of schistosomiasis patients to HBV and HCV might be explained partly, by the transmission of those viruses during transfusion and parenteral therapy for schistosomiasis via contaminated blood, needles, and syringes. Furthermore, studies have shown that the cell-mediated response is depressed in active intestinal schistosomiasis and this immunosuppression increases with the advancement of the disease and development of hepatosplenomegaly. These patients tend to retain HBV and HCV for extended periods and attain carrier state with a better risk of

developing complications including HCC.Schistosoma infections affect the immune reaction in two ways in which may prolong the carrier state of the virus. Anti-idiotype antibodies produced in patients with chronic schistosomiasis can downregulate specific immune responses and suppress nonspecific immune responses. Additionally, various studies in mice and humans have shown that *S. mansoni* egg antigens can modify subpopulations of thymus helper cells. The activity and therefore, the cytokines involved eosinophilia and IgE secretion are stimulated while Th1 activity and the cytokines, IL2 and interferon-gamma, also as CD8+ cytotoxic T cells are downregulated in BALB/C mice infected with *S. mansoni*.

Opisthorchis and Chlonorchis Infections

O. viverrini, *O. felineus*, and *C. Sinensis* are flatworms inhabiting the human liver. They continue to be important public ill-health in many endemic areas where they infect a minimum of 20 million people. Additionally to their association with hepatobiliary disease, they're major aetiological agents of common bile duct cancer. This is often the number one explanation for death in northeast Thailand. The adult hermaphrodite parasites sleep in the smaller intrahepatic bile ducts of their final hosts, which include humans, dogs, cats, and other wild and livestock. Eggs are laid within the biliary system and are excreted within the faeces, which are ingested by the primary intermediate hosts, the Bithynia snails. The eggs hatch inside the snails and eventually mature leaving the snail within the sort of freely swimming cercariae, which successively penetrates the fish, the second host where they become metacercariae. Ingesting raw, pickled, or undercooked fish infects humans. The metacercariaeexcyst within the duodenum and jejunum and migrate through the ampulla of Vater into the common bile duct where they mature into adult flukes which will live there for up to 30 years. The foremost chronically infected individuals have few specific signs or symptoms except an increased frequency of palpable liver. Symptomatic cases generally experience pain within the right upper quadrant of the abdomen, diarrhea, loss of appetite, indigestion, etc. the foremost important complication of *Fasciolahepatica* infection is an enhanced susceptibility tocholangiocarcinoma. After evaluating epidemiological studies, case series, and case-control studies, the IARC concluded that *O. viverrini* may be a definite human carcinogen whereas evidence for the carcinogenic effect of *O. felineus* and *C. Sinensis* is more limited. Many cases of cancer of the liver arising in patients with *O. viverrini* infection are reported from Thailand. In most regions of the planet, cholangiocarcinoma may be a very rare tumor. In areas where *O. viverrini* is endemic, however, the numbers of cases of cholangiocarcinoma generally outnumber those of hepatoma.

Several cross-sectional or case-control studies on the association between *O.*

viverrini infection and cancer of the liver are reported from Thailand. Within the first large case study, a strangely high incidence of cholangiocarcinoma was observed in both the autopsy and biopsy materials taken from the patients with *O. viverrini* infection. The ratio between hepatoma and cholangiocarcinoma in autopsies without opisthorchiasis was 8:1, whereas the ratio was reversed among those with *Fasciolahepatica* infection. Similarly, the ratio of those two malignancies in biopsies was 5:1 in non- infected patients and 1:2 within the presence of the fluke. Similar results are confirmed by other authors who showed that the incidence of cholangiocarcinoma was almost twice that of hepatoma in endemic areas of *O. viverrini* within the north-east of the country, and therefore the incidence in males was 2.4 times that in females. In another case-control study, the *O. viverrini* infection increased the danger of cholangiocarcinoma fivefold.

There is ample evidence that *Clonorchisinensis* is additionally related to cholangiocarcinoma. Cases of cancer of the liver in association with infection with *C. Sinensis* are reported from China, Hong Kong, the Republic of Korea, and Japan and in immigrants to North America from China and Laos. In Pusan, a neighborhood with an extremely high prevalence of *C. Sinensis* the fluke increased the danger of cholangiocarcinomasixfold.Another case-control study within the same area showed that *C. Sinensis* within the stool was significantly related to cholangiocarcinoma with an estimated relative risk of two. Cases of cholangiocarcinoma, related to *C. Sinensis*, have also been reported among Asian immigrants to the USA.

Trichomoniasis

Trichomonasvaginalis may be a pathogenic protozoan, which resides within the lower female genitourinary tract. Infection may or might not be symptomatic. It sexually transmitted and occurs worldwide in both urban and rural populations. In sexually transmitted disease clinics, overall infection rates varying from 7 to 32% are recorded. Highest prevalence figures are in groups with a high level of sexual intercourse. The organism is usually coexistent with other infections like candidiasis, bacterial vaginosis, gonorrhea, or HIV infection. The classical clinical presentation is that of vulvovaginitis with a yellow frothy discharge. Some may have vulval irritation or dyspareunia. In men, the majority of infections are asymptomatic although few may present as NGU.

Many researchers have studied the association between *T. vaginalis* infection and cervical neoplasia. Most studies have shown an association between *T. vaginalis* and risk of cervical neoplasm through a cause and effect relationship has not been proven. Few studies, however, have shown no association between the 2. The proof of association comes from either serological or histopathological studies. Antibodies to *T. vaginalis* are detected in 18 to 43% of invasive cervical neoplasia compared with only 5% within the control groups and

therefore the risk ratio was found to be 3. The rise in antibody titer was especially evident within the 40-49 year age bracket and in patients with epithelial cell carcinoma especially grade II and III. In an analysis of obtainable data from studies on the association between i. *vaginalis* infection and cervical neoplasia, a complete of 24 studies (2 cohorts and 22 case-control) were included. The combined summary relative risk for the 2 cohort studies was 1.93 indicating an approximate doubling of the danger of cervical neoplasia in the presence of *T*. vaginalis infection. The attributable risks among exposed subjects and source populations were 47.4% and 2.15% respectively. Results of the 22 retrospective studies are much less consistent, however, most of those demonstrated a big positive association.

Toxoplasmosis

There are a couple of reports within the literature about the connection between *Toxoplasmagondii* infection and tumors including primary ocular tumors, meningioma, leukemia and lymphoma. Zhang *et al* described two cases of pituitary adenoma related to *T. gondii*. The toxoplasma cysts were found among the tumor cells and were verified using *T. gondii* specific antibody by immunohistochemistry. In another study investigated in two parts, one based in Adelaide, South Australia, and therefore the other based in Melbourne, Victoria, all tumors were verified histologically and IgG antibodies to *T. gondii* were measured by ELISA. Both studies suggest that the possession of antibody to *T. gondii* is unlikely to be a risk factor for glioma. The Adelide study provides some evidence that seropositivity could also be related to meningioma.48 it's been demonstrated in experimental studies that exogenous prolactin has antiparasitic effects. Thus, the idea has been suggesting that overstimulation of the pituitary to fight the parasitic infection, may cause adenoma formation. However, no further research regarding the role of *Toxoplasma* in tumorigenesis has been reported.

CONCLUSION

In summary, whereas some parasitic infections like *O. viverrini* and*S.haematobium* are very strongly related to cancers and are an important predisposing factor for specific cancers; other parasites may have a probable role in the development of certain cancers. Early diagnosis, prompt treatment, and prevention of such infections may help in a significant reduction in the occurrence of those cancerous conditions.

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